

### **AMENDMENTS TO THE SPECIFICATION**

**Please amend paragraph number [00049] as follows:**

**[00049]** The term "heteroatom-containing" as in a "heteroatom-containing hydrocarbonyl group" refers to a molecule or molecular fragment in which one or more carbon atoms is replaced with an atom other than carbon, e.g., nitrogen, oxygen, sulfur or phosphorus. Similarly, the term "heteroalkyl" refers to an alkyl substituent that is heteroatom-containing, the term "heterocyclic" refers to a cyclic substituent that is heteroatom-containing, the term "heteroaryl" refers to an aryl substituent that is heteroatom-containing, and the like. Heteroatoms can also replace certain carbon atoms as part of unsaturated systems such as wherein an oxygen atom replaces a carbon atom in an alkene to generate a ketone or aldehyde, and wherein a nitrogen atom replaces a carbon atom in an alkyne to generate a nitrile. Examples of common heteroatom-substituted radicals used in nucleotide chemistry are  $\beta$ -cyanoethyl, methyl- $\beta$ -cyanoethyl, dimethyl- $\beta$ -cyanoethyl, phenylsulfonyl, methyl-sulfonyl, *p*-nitrophenylsulfonyl, 2,2,2-trichloro-1,1-dimethylethyl, 2-(4-pyridyl)ethyl, 2-(2-pyridyl)ethyl,  $\beta$ -thiobenzoyl, 1,1,1,3,3,3-hexafluoro-2-propyl, 2,2,2-trichloroethyl, *p*-nitrophenylethyl, *p*-cyanophenylethyl, acetyl, tetrahydropyranyl, di-*p*-methoxytrityl, and benzoyl radicals. When the term "heteroatom-containing" appears prior to a list of possible heteroatom-containing groups, it is intended that the term apply to every member of that group.

**Please amend paragraph number [00059] as follows:**

**[00059]** The term "elimination reaction" as used herein is meant to describe a chemical reaction by which a species is removed by "elimination" or "fragmentation." This is in contrast to an operation by which a species is removed by a "substitution reaction." An example of this distinction is the contrast between the typical method for the removal of an ethyl group from a protected carboxylic acid (i.e., an ethyl ester) using a hydroxide nucleophile, and the removal of a  $\beta$ -cyanoethyl blocking group from a protected carboxylic acid (i.e., a  $\beta$ -cyanoethyl ester) using a non-nucleophilic base. The ethyl-protected carboxylic acid is deprotected by substitution of the ethoxide group on the carbonyl group of the ester with hydroxide, whereas the  $\beta$ -cyanoethyl-protected carboxylic acid is deprotected by elimination or fragmentation as the protecting group

is transformed by specific chemical reactions leaving the carboxylate intact. With the  $\beta$ -cyanoethyl protecting group, the specific chemical reaction is base-catalyzed  $\beta$ -elimination. There are many other protecting groups, well known to those skilled in the art, which may be removed by elimination or fragmentation, leaving the carboxylate moiety intact, rather than by substitution on the carbonyl. Examples of protecting groups that may be removed by elimination reactions, by way of illustration and not limitation, are:  $\beta$ -cyanoethyl, methyl- $\beta$ -cyanoethyl, dimethyl- $\beta$ -cyanoethyl, phenylsulfonylethyl, methyl-sulfonylethyl, *p*-nitrophenylsulfonylethyl, 2,2,2-trichloro-1,1-dimethylethyl, 2-(4-pyridyl)ethyl, 2-(2-pyridyl)ethyl, allyl, 4-methylene-1-acetylphenol,[[.]] $\beta$ -thiobenzoylethyl, 1,1,1,3,3,3-hexafluoro-2-propyl, 2,2,2-trichloroethyl, *p*-nitrophenylethyl, *p*-cyanophenyl-ethyl, 9-fluorenylmethyl, 1,3-dithionyl-2-methyl, 2-(trimethylsilyl)ethyl, 2-methylthioethyl, 2-(diphenylphosphino)-ethyl, 1-methyl-1-phenylethyl, 3-buten-1-yl, 4-(trimethylsilyl)-2-buten-1-yl, cinnamyl, -methylcinnamyl, and 8-quinolyl.

**Please amend paragraph number [00066] as follows:**

[00066] R<sup>1</sup> is hydrogen, a protecting group removable by an elimination reaction, hydrocarbyl, substituted hydrocarbyl, heteroatom-containing hydrocarbyl or substituted heteroatom-containing hydrocarbyl. Preferably, R<sup>1</sup> is hydrogen or an unsubstituted, substituted, heteroatom-containing or substituted heteroatom-containing moiety selected from the group consisting of alkyl, aryl, aralkyl, alkaryl, cycloalkyl, cycloalkylalkyl, cycloalkylaryl, alkenyl, cycloalkenyl, aralkenyl, alkynyl and aralkynyl. R<sup>1</sup> may also be a protecting group, in which case it is removable by an elimination reaction. Protecting groups suitable for use as R<sup>1</sup> will generally although not necessarily be: electron-withdrawing -substituted aliphatic groups, particularly electron-withdrawing -substituted ethyl; electron-withdrawing substituted phenyl; and electron-withdrawing substituted phenylethyl. Specific examples of suitable protecting groups include, by way of example,  $\beta$ -cyanoethyl, methyl- $\beta$ -cyanoethyl, dimethyl- $\beta$ -cyanoethyl, phenylsulfonylethyl, methyl-sulfonylethyl, *p*-nitrophenylsulfonylethyl, 2,2,2-trichloro-1,1-dimethylethyl, 2-(4-pyridyl)ethyl, 2-(2-pyridyl)ethyl, allyl, 4-methylene-1-acetylphenol,[[.]] $\beta$ -thiobenzoylethyl, 1,1,1,3,3,3-hexafluoro-2-propyl, 2,2,2-trichloroethyl, *p*-nitrophenylethyl, *p*-cyanophenyl-ethyl, 9-fluorenylmethyl, 1,3-dithionyl-2-methyl, 2-(trimethylsilyl)ethyl,

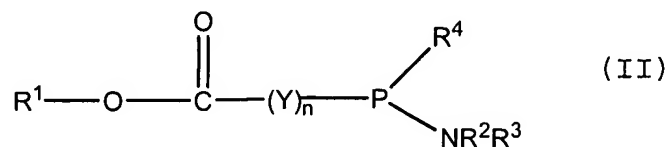
2-methylthioethyl, 2-(diphenylphosphino)ethyl, 1-methyl-1-phenylethyl, 3-buten-1-yl, 4-(trimethylsilyl)-2-buten-1-yl, cinnamyl, -methylcinnamyl, and 8-quinolyl.

**Please amend paragraph number [00068] as follows:**

[00068]  $R^4$  is  $NR^5R^6$ , halogen or DL, wherein  $R^5$  and  $R^6$  are as defined above for  $R^2$  and  $R^3$ , D is O, S or NH, preferably O, and L is a heteroatom-protecting group, unsubstituted hydrocarbyl, substituted hydrocarbyl, heteroatom-containing hydrocarbyl, or substituted heteroatom-containing hydrocarbyl. When L is a heteroatom-protecting group, it is removable by an elimination reaction. Examples of heteroatom-protecting groups that can serve as L include, but are not limited to, those groups recited as suitable  $R^1$  protecting groups that are removable by an elimination reaction, i.e.  $\beta$ -cyanoethyl, methyl- $\beta$ -cyanoethyl, dimethyl- $\beta$ -cyanoethyl, phenylsulfonyl-ethyl, methyl-sulfonyl-ethyl, *p*-nitrophenyl-sulfonyl-ethyl, 2,2,2-trichloro-1,1-dimethylethyl, 2-(4-pyridyl)ethyl, 2-(2-pyridyl)ethyl, allyl, 4-methylene-1-acetylphenol,  $[\beta$ -thiobenzoyl-ethyl, 1,1,1,3,3,3-hexafluoro-2-propyl, 2,2,2-trichloroethyl, *p*-nitrophenylethyl, *p*-cyanophenyl-ethyl, 9-fluorenylmethyl, 1,3-dithionyl-2-methyl, 2-(trimethylsilyl)ethyl, 2-methylthioethyl, 2-(diphenylphosphino)ethyl, 1-methyl-1-phenylethyl, 3-buten-1-yl, 4-(trimethylsilyl)-2-buten-1-yl, cinnamyl, -methylcinnamyl and 8-quinolyl.

**Please amend paragraph number [00073] as follows:**

[00073] In a particularly preferred embodiment, then, the phosphinoamidite carboxylate has the structure of formula (II)



wherein:  $R^1$  is hydrogen, lower alkyl, or a hydroxyl-protecting group removable by an elimination reaction, preferably although not necessarily an electron-withdrawing -substituted aliphatic group;  $R^2$  and  $R^3$  are lower alkyl, e.g., isopropyl, or  $R^2$  and  $R^3$  are linked to form a piperidino, piperazino or morpholino ring;  $R^4$  is  $NR^5R^6$ , chloro or OL wherein  $R^5$  and  $R^6$  are as

defined for  $R^2$  and  $R^3$ , and L is a hydroxyl-protecting group removable by an elimination reaction, generally although not necessarily selected from the group consisting of  $\beta$ -cyanoethyl, methyl- $\beta$ -cyanoethyl, dimethyl- $\beta$ -cyanoethyl, phenylsulfonyl-ethyl, methylsulfonyl-ethyl, *p*-nitrophenyl-sulfonyl-ethyl, 2,2,2-trichloro-1,1-dimethylethyl, 2-(4-pyridyl)ethyl, 2-(2-pyridyl)ethyl, allyl, 4-methylene-1-acetylphenol,  $\beta$ -thiobenzoyl-ethyl, 1,1,1,3,3,3-hexafluoro-2-propyl, 2,2,2-trichloroethyl, *p*-nitrophenylethyl, *p*-cyanophenyl-ethyl, 9-fluorenylmethyl, 1,3-dithionyl-2-methyl, 2-(trimethylsilyl)ethyl, 2-methylthioethyl, 2-(diphenylphosphino)ethyl, 1-methyl-1-phenylethyl, 3-buten-1-yl, 4-(trimethylsilyl)-2-buten-1-yl, cinnamyl, -methylcinnamyl and 8-quinolyl; n is zero or 1; and Y is  $-(Y')_m-(CH_2)-$  wherein m is zero or 1 and Y' is lower alkylene, with the proviso that when n is 1 and m is zero, then  $R^1$  is either hydrogen or a hydroxyl-protecting group.